



UNITED STATES PATENT AND TRADEMARK OFFICE

 COMMISSIONER FOR PATENTS
 UNITED STATES PATENT AND TRADEMARK OFFICE
 WASHINGTON, D.C. 20231
 www.uspto.gov

| APPLICATION NUMBER | FILING DATE | GRP ART UNIT | FIL FEE REC'D | ATTY. DOCKET NO | DRAWINGS | TOT CLAIMS | IND CLAIMS |
|--------------------|-------------------------------------|--------------|---------------|-----------------|----------|------------|------------|
| 09/642,557 | 08/16/2000 05/18/2000 | 1621 | 0 | 860098.436 | 7 | 24 | 3 |

Karl R Hermanns
 Seed Intellectual Property Law Group PLLC
 701 Fifth Avenue
 Suite 6300
 Seattle, WA 98104-7092

FILING RECEIPT



OC00000005516673

RECEIVED

NOV 06 2000

 SEED INTELLECTUAL PROPERTY
 LAW GROUP PLLC

Date Mailed: 10/30/2000

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the PTO processes the reply to the Notice, the PTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Brydon L. Bennett et. al., Residence Not Provided;

→ Brydon L. Bennett, San Diego, CA;
 Shripad S. Bhagwat, San Diego, CA;
 Anthony M. Manning, San Diego, CA;
 Brion W. Murray, San Diego, CA;
 Eoin C. O'Leary, San Diego, CA; and
 Yoshitaka Satoh, San Diego, CA.

Continuing Data as Claimed by Applicant

This application claims the benefit of
 Foreign Applications provisional application no.
 60/240,928, filed August 19, 1999.

If Required, Foreign Filing License Granted 10/30/2000

Title

Pyrazoloanthrone and derivatives thereof as JNK inhibitors and compositions and methods
 related thereto

Preliminary Class

548

Data entry by : HARRISON, BRUCE

Team : OIPE

Date: 10/30/2000



**LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15**

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 36 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (j)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15 (b).

PLEASE NOTE the following information about the Filing Receipt:

- The articles such as "a," "an" and "the" are not included as the first words in the title of an application. They are considered to be unnecessary to the understanding of the title.
- The words "new," "improved," "improvements in" or "relating to" are not included as first words in the title of an application because a patent application, by nature, is a new idea or improvement.
- The title may be truncated if it consists of more than 600 characters (letters and spaces combined).
- The docket number allows a maximum of 25 characters.
- If your application was submitted under 37 CFR 1.10, your filing date should be the "date in" found on the Express Mail label. If there is a discrepancy, you should submit a request for a corrected Filing Receipt along with a copy of the Express Mail label showing the "date in."
- The title is recorded in sentence case.

Any corrections that may need to be done to your Filing Receipt should be directed to:

Assistant Commissioner for Patents
Office of Initial Patent Examination
Customer Service Center
Washington, DC 20231





UNITED STATES PATENT AND TRADEMARK OFFICE

 COMMISSIONER FOR PATENTS
 UNITED STATES PATENT AND TRADEMARK OFFICE
 WASHINGTON, D.C. 20231
 www.uspto.gov

3

| APPLICATION NUMBER | FILING/RECEIPT DATE | FIRST NAMED APPLICANT | ATTORNEY DOCKET NUMBER |
|--------------------|---------------------|---------------------------|------------------------|
| 09/642,557 | 08/16/2000 | Brydon L. Bennett et. al. | 860098.436 |

FORMALITIES LETTER



OC000000005516674

Karl R Hermanns
 Seed Intellectual Property Law Group PLLC
 701 Fifth Avenue
 Suite 6300
 Seattle, WA 98104-7092

Date Mailed: 10/30/2000

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given TWO MONTHS from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
Applicant must submit \$ 690 to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).
- Total additional claim fee(s) for this application is \$72.
 - \$72 for 4 total claims over 20.
- The oath or declaration is missing.
A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Application Number and Filing Date, is required.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of \$130 for a non-small entity, must be submitted with the missing items identified in this letter.
- The balance due by applicant is \$ 892.

 03/23/2001 GDEBELA1 00000071 161150 09642557 *A copy of this notice MUST be returned with the reply.*

| | |
|-----------|-----------|
| 01 FC:201 | 355.00 CH |
| 02 FC:203 | 36.00 CH |
| 03 FC:205 | 65.00 CH |

Customer Service Center

Initial Patent Examination Division (703) 308-1202

PART 1 - ATTORNEY/APPLICANT COPY



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

Applicants : Brydon L. Bennett; Shripad S. Bhagwat; Anthony M. Manning;
Brion W. Murray; Eoin C. O'Leary; Yoshitaka Satoh
Filed : August 18, 2000
For : PYRAZOLOANTHRONE AND DERIVATIVES THEREOF AS
JNK INHIBITORS AND COMPOSITIONS AND METHODS
RELATED THERETO

Docket No. : 860098.436

Date : August 18, 2000

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Assistant Commissioner for Patents:

I hereby certify that the enclosures listed below are being deposited with the United States Postal Service "EXPRESS MAIL Post Office to Addressee" service under 37 C.F.R. § 1.10, Mailing Label Certificate No. EL487464460US, on August 18, 2000, addressed to Box Patent Application, Assistant Commissioner for Patents, Washington, DC 20231.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC

Steve Plante

KRH:lm.

Enclosures:

Postcard
Form PTO/SB/05
Specification, Claims, Abstract (62 pages)
7 Sheets of Drawings (Figures 1-5)

\\VERNON\USERS\LindaM\00-2\8310.doc



Express Mail No. **EL 501 638 098 US**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Bennett et al.

Serial No.: 09/642,557

Group Art Unit: 1621

Filed: August 18, 2000

Examiner: To be Assigned

For: PYRAZOLOANTHRONE AND
DERIVATIVES THEREOF AS JNK
INHIBITORS AND
COMPOSITIONS AND METHODS
RELATED THERETO

Attorney Docket No.: 10624-046-999

REQUEST FOR CORRECTION OF FILING RECEIPT

Assistant Commissioner for Patents
Office of Initial Patent Examination
Customer Service Center
Washington, DC 20231

Sir:

Enclosed is the original and one copy of the filing receipt for the present application.

Please note the errors where highlighted on the copy of the filing receipt:

The filing date is incorrect. As evidenced by the Certificate of Mailing (a copy being enclosed) and Express Mail receipt (a copy being enclosed) for the present application, the correct filing date is **August 18, 2000**.

The Applicant(s) information is incorrect. As evidenced by the Declaration filed concurrently herewith, the correct Applicant(s) information is:

Brydon L. Bennett, San Diego, California;

Shripad S. Bhagwat, San Diego, California;

Anthony M. Manning, San Diego, California;

Brion W. Murray, San Diego, California;



Express Mail No.: EL 501 638 098 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Bennett et al.

Application No.: 09/642,557

Group Art Unit: 1621

Filed: August 18, 2000

Examiner: To be assigned

For: PYRAZOLOANTHRONE AND
DERIVATIVES THEREOF AS JNK
INHIBITORS AND
COMPOSITIONS AND METHODS
RELATED THERETO

Attorney Docket No.: 10624-046-999

**REQUEST TO ESTABLISH SMALL ENTITY STATUS
AND TRANSMITTAL OF VERIFIED STATEMENT CLAIMING
SMALL ENTITY STATUS UNDER 37 C.F.R. §1.9(f) and 1.27(c)(d)**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Attorneys for Applicants request that Small Entity Status be established and submit herewith an original executed Verified Statement Claiming Small Entity Status - Small Business Concern from SIGNAL PHARMACEUTICALS, INC., assignee of the above-identified application. It is requested that this document be made of record in the file of the above-identified application.

Date March 21, 2001

Respectfully submitted,

Anthony M. Insogna, N.Y. No. 35,203
By Matthew E. Luger, N.Y. No. 36,343
35,203

Anthony M. Insogna

(Reg. No.)

PENNIE & EDMONDS LLP

1155 Avenue of the Americas

New York, New York 10036-2711

(212) 790-9090



Eoin C. O'Leary, San Diego, California; and

Yoshitaka Satoh, San Diego, California.

The Continuing Data as claimed by Applicant is incorrect. As evidenced by the present application, page 1 (a copy being enclosed), and a petition (a copy being enclosed) granted in connection with parent application no. 09/378,234 (the "234 application"), filed August 19, 1999, converting the '234 application to provisional application no 60/240,928, the correct data are as follows:

This application claims the benefit of provisional application no. 60/240,928, filed August 19, 1999.

Please correct these errors as soon as possible.

To the extent that these errors are on the part of the Patent Office, no fee should be charged to us. However, should the Patent Office determine otherwise, please charge the necessary fee to Pennie & Edmonds LLP Deposit Account no. 16-1150. A duplicate of this sheet is enclosed.

Respectfully submitted,

Anthony M. Insogna, N.Y. No. 35,203
By Matthew E. Langer, N.Y. No. 36,343

Date: March 21, 2001

Anthony M. Insogna

35,203
(Reg. No.)

PENNIE & EDMONDS LLP

1155 Avenue of the Americas

New York, New York 10036-2711

(212) 790-9090



Express Mail No.: EL 501 638 098 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Bennett et al.

Application No.: 09/642,557

Group Art Unit: 1621

Filed: August 18, 2000

Examiner: To Be Assigned

For: PYRAZOLOANTHRONE AND
DERIVATIVES THEREOF AS JNK
INHIBITORS AND
COMPOSITIONS AND METHODS
RELATED THERETO

Attorney Docket No.: 10624-046-999

**RESPONSE TO NOTICE TO FILE MISSING PARTS
OF NON-PROVISIONAL APPLICATION FILED UNDER 37 C.F.R. §1.53(b)**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notice to File Missing Parts of Non-Provisional Application, which was mailed on October 30, 2000 (a copy of which is attached hereto), Attorneys for Applicants respectfully submit herewith a Declaration executed by the present inventors, Brydon L. Bennett, Shripad S. Bhagwat, Anthony M. Manning, Brion W. Murray, Eoin C. O'Leary and Yoshitaka Satoh.

Also submitted herewith is an Assignment of rights from the inventors to Signal Pharmaceuticals, Inc. and a recordation form cover sheet with provision for the required fee.

Also submitted herewith is a Power of Attorney by Assignee and Exclusion of Inventors Under 37 C.F.R. §3.71 executed by David W. Anderson, Chief Scientific Officer of Signal Pharmaceuticals, Inc.

Also submitted herewith is a Request to Establish Small Entity Status and Transmittal of Verified Statement Claiming Small Entity Status, along with a Verified Statement of David W. Anderson, Chief Scientific Officer, Signal Pharmaceuticals, Inc.

Also submitted herewith is a Petition for an Extension of Time for three (3) months, up to and including March 30, 2001, with provision for the required fee.

Attorneys for Applicants submit the required basic filing fee (as a Small Entity) (estimated to be \$355.00), plus the surcharge for a small entity (estimated to be \$65.00), and plus additional claim fees for 4 total claims over 20 (estimated to be \$36.00) for an estimated total of \$456.00. Please charge the required fees to Pennie & Edmonds LLP Deposit Account No. 16-1150. A copy of this paper is submitted herewith for accounting purposes.

Applicants respectfully request that the above-identified documents be made of record in the present application file.



Date March 21, 2001

Respectfully submitted,

Anthony M. Insogna, Reg. No. 35,203
By Anthony M. Insogna, Reg. No. 36,343
35,203

Anthony M. Insogna

(Reg. No.)

PENNIE & EDMONDS LLP

1155 Avenue of the Americas

New York, New York 10036-2711

(212) 790-9090



PYRAZOLOANTHRONE AND DERIVATIVES THEREOF AS JNK INHIBITORS
AND COMPOSITIONS AND METHODS RELATED THERETO

CROSS-REFERENCE TO RELATED APPLICATION

- 5 This application claims the benefit of U.S. Application No. 09/378,234 filed August 19, 1999 (incorporated by reference in its entirety), which application was converted to U.S. Provisional Application No. (awaiting) by petition filed August 16, 2000.

TECHNICAL FIELD

- 10 This invention is generally directed to pyrazoloanthrone and derivatives thereof which have utility over a wide range of indications, including activity as Jun N-terminal kinase inhibitors, and related compositions and methods.

BACKGROUND OF THE INVENTION

- 15 The Jun N-terminal kinase (JNK) pathway is activated by exposure of cells to environmental stress or by treatment of cells with pro-inflammatory cytokines. Targets of the JNK pathway include the transcription factors c-jun and ATF2 (Whitmarsh A.J., and Davis R.J. *J. Mol. Med.* 74:589-607, 1996). These transcription factors are members of the basic leucine zipper (bZIP) group that bind as homo- and hetero-dimeric complexes to AP-
20 1 and AP-1-like sites in the promoters of many genes (Karin M., Liu Z.G. and Zandi E. *Curr Opin Cell Biol* 9:240-246, 1997). JNK binds to the N-terminal region of c-jun and ATF-2 and phosphorylates two sites within the activation domain of each transcription factor (Hibi M., Lin A., Smeal T., Minden A., Karin M. *Genes Dev.* 7:2135-2148, 1993; Mohit A.A., Martin M.H., and Miller C.A. *Neuron* 14:67-75, 1995). Three JNK enzymes
25 have been identified as products of distinct genes (Hibi et al, *supra*; Mohit et al., *supra*). Ten different isoforms of JNK have been identified. These represent alternatively spliced forms of three different genes: JNK1, JNK2 and JNK3. JNK1 and 2 are ubiquitously expressed in human tissues, whereas JNK3 is selectively expressed in the brain, heart and testis (Dong, C., Yang, D., Wysk, M., Whitmarsh, A., Davis, R., Flavell, R. *Science* 270:1-